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ORIGINAL RESEARCH

Nurse evaluation of the redesigned fertility pen injector: a questionnaire-based observational survey

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ABSTRACT

Background: Owing to the wide-ranging role nurses have in supporting patients undergoing fertility treatment, we recorded the learning/teaching expectations and experiences of nurses using a redesigned fertility pen injector.

Methods: This was a multicentre, simulated-use study, using unbranded placebo-filled pens. Before teaching patients, nurses were given free choice to rank the importance of the device attributes and predict the level of patient anxiety. Nurses taught 2–5 patients how to prepare the device, inject the dose and complete an incomplete dose. They rated the teaching experience on a 5-point scale during a questionnaire interview.

Results: Thirty nurses were enrolled across four countries. All nurses found the redesigned fertility pen injector easy to use and teach. 90% found the overall administration process easy to learn and teach. More than 80% (range 83%–100%) found each of the steps easy (score 4 or 5), and most found the steps easier to teach than expected (score 4 or 5; range 57%–90%). 97% would recommend the redesigned fertility pen injector to a colleague.

Conclusions: Nurses rated the redesigned fertility pen injector easy to learn and use and easier to teach than expected. Most would recommend the device to a colleague.

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KEYWORDS
ART; follitropin alfa; GONAL-f; IVF; nurses; patients; pen injector; questionnaire

1. Introduction

Patients embarking on infertility treatment or assisted reproductive technologies (ART) are highly motivated to achieve treatment success, and infertility/ART treatments have helped many couples to have children. GONAL-f® (recombinant human follicle-stimulating hormone [r-hFSH]; follitropin alfa; Merck KGaA, Darmstadt, Germany) first gained marketing authorization more than 20 years ago. Since then, for women, the cumulative patient exposure to GONAL-f is estimated at around 13,757,736 treatment-cycles in the post-marketing setting [1]. Assuming a conservative live-birth rate estimate of around 20% per cycle, this represents more than 2.75 million babies born with the support of GONAL-f [2].

Despite this success, there is still a high rate of patient dropout from fertility treatment [3,4]. Several reasons have been cited for this, including the emotional distress and discomfort due to the demanding and complicated treatment regimens, and anxiety about multiple injections, the use of needles and correct dosing when using injected treatments [3–8]. The use of pen injectors may help to alleviate some of these concerns. Pen injectors are more accurate, easier and quicker to use and more discrete than syringe and vial, and their use is also less stressful and can result in fewer injection-site adverse events, leading to better compliance to treatment [9–12]. In addition, compared with syringe and vial, pen injectors have been shown to reduce needle fear/aversion and require fewer steps to prepare, limiting the potential for reduced efficacy due to reconstitution or dosing errors [13–17].

Manufacturers continually update the design of pen injectors. The aim of this is to improve the ease of handing and to make the pen injectors easier and more comfortable to use, and thus improve patient confidence [18–20]. A pen injector for the delivery of GONAL-f first became available in 2005 [13,21] and, in the period since its introduction, the design of this pen injector has been continuously refined and updated, with the most recent version approved by the European Medicines Agency in June 2016 [22] and the US Food and Drug Administration in November 2017 [23]. This latest version has improved robustness, handling, and readability of the dose-feedback window compared with the previous version [15]. It also provides feedback that the correct dose has been administered or displays the remaining dose that may need to be injected with a second device. The associated instructions for use (IFU) and the teaching video were also modified to reflect these changes.

This redesigned pen injector provides a platform for the delivery of a range of fertility treatments, including GONAL-f and the liquid formulation of combined recombinant human follitropin alfa and recombinant human luteinizing hormone

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Supplemental data for this article can be accessed here.

(Pergoveris®; lutropin alfa; Merck KGaA, Darmstadt, Germany), approved by the European Medicines Agency in May 2017 to replace the freeze-dried formulation, which required reconstitution and syringe injection [22].

Summative evaluation has shown that this redesigned pen injector and associated materials can be used safely and effectively to perform critical tasks related to administering the required dose that were identified during the risk-management assessments [24,25]. The dose accuracy of the redesigned pen injector was also confirmed under a range of conditions, including cold, standard and warm environments and subsequent to free fall, vibration, dry-heat, cold storage, and shipping preconditioning [26]. The ease of learning to use and ensuing use of the redesigned fertility pen injector by women with recent or current infertility requiring ART or IVF was also investigated as well as their overall impressions of learning to use and using the redesigned fertility pen injector [27]. Both ART/IVF-experienced and ART/IVF-naïve women found the pen injector easy to learn to use and easy to use. These summative evaluations were carried out using unbranded placebo-filled redesigned pen injectors.

Owing to the substantial and varied role infertility nurses have in the treatment of patients with infertility, encompassing patient orientation, education, counseling and support, and treatment planning and coordination [14], they are the most likely healthcare provider to teach patients to self-inject [14]. Such teaching is generally conducted in-person and involves both the person with infertility and their partner, although this may be supported by additional group classes. Nurses, therefore, have a considerable influence on pen injector use [20], and fertility nurse assessment of the ease of use and ease of teaching patients on new or redesigned pen injectors is an important factor in the development of these devices.

As a further assessment of the safe and effective use of the redesigned fertility pen injector, the study reported here is a simulated-use study of this device that included fertility nurses and women with infertility. The aim was to evaluate the ease of use and the subsequent teaching of ART/IVF-experienced and ART/IVF-naïve women with infertility by fertility nurses.

2. Participants and methods

2.1. Study participants

This study recruited fertility nurses and women with infertility. Fertility nurses were working in fertility clinics, hospitals, or both, and were responsible for teaching women undergoing fertility treatment to use self-injection devices. Nurses had to see at least 15 patients with infertility per month and to teach at least five patients per month to use self-injection devices. Opinions were collected from nurses during a questionnaire interview before and after they taught any of the women with infertility (Appendix A). The patient cohort comprised women of reproductive age (18–45 years) with infertility who were either currently seeking ART treatment (ART/IVF-naïve) or had undergone ART/IVF in the past 6 months or were currently in treatment (ART/IVF-experienced).

2.2. Design and setting

This was a simulated-use study conducted in France, Italy, Spain, and the UK between December 2015 and March 2016. The protocol was approved internally by the sponsors before the study started. All participants provided written informed consent. Institutional Review Board or Independent Ethics Committee approval was not required because this was a nonclinical, simulated-use study, with all injections performed into artificial-skin injection pads.

Placebo-filled, non-branded demonstration versions of the redesigned fertility pen injector were used in the study. Because this version has only been approved since June 2016, the participants would have had no previous experience with this version of the pen injector. The participants were not aware of the company sponsoring the study or of the drugs with which the redesigned fertility pen injector was intended for use.

Participants also had access to the unbranded updated IFU for the redesigned pen injector, which describes the injection process in seven distinct steps, with an appendix (Appendix A) containing instructions for completing an incomplete dose (Table 1). This study evaluated perceptions of steps 3–6, Appendix A and the constituent sub-steps, all of which were identified in the risk-management plan for their potential for use errors. The risk-management plan was implemented to identify hazards associated with use, estimate and evaluate risks, and develop, implement, and monitor risk-control measures [28].

2.3. Teaching procedures and study questionnaires

Before undergoing training, nurses were given free choice to predict the anxiety that would be felt by the women with infertility when using the device. The nurse participants were then taught by a moderator in a session lasting 15–20 min. Each

Table 1. Steps from the instructions for use referring to completing an injection with the redesigned fertility pen injector.

Step	Instructions
Step 1	Get ready • Wash and dry hands • Remove pen and needle from carton • Check expiration date on pen label
Step 2	Choose and prepare your injection site • Select injection site • Wipe skin with alcohol wipe
Step 3	Attach your needle • Remove pen cap • Check reservoir • Attach needle • Remove needle cap • Prime pen (if appropriate)
Step 4	Dial your dose
Step 5	Inject your dose • Confirm dose in dose-feedback window • Push needle into skin • Press dose knob • Remove needle from skin • Release dose knob • Confirm the number displayed in the dose-feedback window
Step 6	Remove and discard needle
Step 7	Record injection in treatment diary
Appendix A	Complete an incomplete dose if necessary

nurse subsequently taught 2–5 patients on the use of the redesigned fertility pen injector during a 45-min session, of which 15–20 min was allocated to training patients to use the device. The IFU was referred to during teaching and was available throughout the study. Nurses completed the evaluation questionnaire (**Supplementary appendix**) after they had taught patients and rated out of ten the attributes of the injection device that they considered to be the most important.

2.4. Statistical analysis

Data from the questionnaire were reported using descriptive statistics. Scales to rate key performance indicators used a 5-point scale, where 1 was the most negative and 5 was the most positive. Participants were able to also provide a response of 'Don't Know' for questions determining the overall impression of the redesigned fertility pen injector. The responses to questions investigating participant opinions are quoted as the proportion of participants who provided each response; percentages are rounded up for clarity of reporting.

3. Results

3.1. Study participants

A total of 30 fertility nurses were enrolled, of whom 13 (43%) were fertility nurses working in a hospital, 14 (47%) worked in a fertility clinic, and 3 (10%) worked in both a hospital and a fertility clinic (Table 2). A total of 3 nurses (10%) were based in France, 10 (33%) were based in Italy, 11 (37%) were based in Spain, and 6 (20%) were based in the UK.

The nurses saw a mean of 100 patients per month, and 20 (67%) taught more than 16 patients per month on the use of self-injection devices. All of the nurses had taught patients to use the previous version of the pen injector, and the majority of nurses had also taught patients to inject Menopur® (menotropin; Ferring Pharmaceuticals Ltd, West Drayton, UK) and to use the Puregon® (follitropin beta; Merck Sharp & Dohme, Hoddesdon, UK) pen injector (24 [80%] and 21 [70%], respectively; Table 2). This experience was reflected in the nurses' rating of familiarity with pen injectors: nurses were most familiar with the previous GONAL-f and Puregon pen injectors and least familiar with the Ovaleap® (follitropin alfa; Teva Pharma B.V., Harlow, UK] pen injector and with use of Bravelle® (urofollitropin; Ferring Pharmaceuticals Ltd, West Drayton, UK). None of the nurses required the full time allotted for training in the use the pen.

The nurses instructed a total of 86 women with infertility. Of these, 65 had previously received (53 [62%]) or were currently receiving (12 [14%]) IVF with one or more devices: 41 (63%) with a multiuse disposable pen injector, 30 (46%) with a single-use disposable pen injector, 28 (43%) with a syringe and drug vial, 13 (20%) with a prefilled syringe and 11 (17%) with a reusable device [27].

3.2. Pre-teaching expectations of nurses

The ease of learning how to use the redesigned fertility pen injector (mean score of 6.5 out of 10), the ease of reading the dosing scale (mean score of 6.1 out of 10), and the ease of setting the correct dose (mean score of 5.4 out of 10) were judged as the most important (Figure 1).

When considering their experience, and given a free choice of responses, the nurses considered that the operations of injection devices involved in dialing the correct dose (11 mentions), the size of the dose-feedback window (7 mentions) and having to split a dose over more than one injection (6 mentions) were the aspects that would lead to the most errors (Table 3). Similarly, nurses predicted that patients would be most anxious about adjusting or setting the dose (20 mentions) and knowing whether the full dose had been administered (8 mentions) (Table 4).

Table 2. Fertility nurse demographics.

	n (%)
Region	
France	3 (10%)
Italy	10 (33%)
Spain	11 (37%)
UK	6 (20%)
Specialty	
Fertility nurse	13 (43%)
Nurse working in a fertility clinic	14 (47%)
Nurse working in a fertility clinic and in a hospital as a fertility nurse	3 (10%)
Number of patients seen per month	
15–50	12 (40%)
51–100	10 (33%)
101–200	4 (13%)
201+	4 (13%)
Visual aids	
Long-distance glasses only	4 (13%)
Reading glasses only	5 (17%)
Long-distance and reading glasses	2 (7%)
Long-distance glasses and contact lenses	2 (7%)
Reading glasses and contact lenses	1 (3%)
Contact lenses only	2 (7%)
No visual aids	14 (47%)
Patients taught per month on current devices	
5–7	3 (10%)
8–10	2 (7%)
11–15	5 (16%)
16+	20 (67%)
Experience of teaching patients in the use of injectable treatments	
GONAL-f	30 (100%)
Menopur	24 (80%)
Puregon	21 (70%)
Pergoveris	10 (33%)
Elonva (UK)	10 (33%)
Bemfola	9 (30%)
Luveris	8 (27%)
Fostimon	5 (17%)
Merional (not France)	3 (11%)
Bravelle (not France)	2 (7%)

$N = 30$.

3.3. Post-teaching findings

3.3.1. Overall process of administering

All nurses considered the redesigned fertility pen injector to be easy to use (score 4 or 5) and to teach patients to use (Figure 2). Twenty-seven nurses (90%) found that, overall, teaching patients was easier than they expected it to be (score 4 or 5). Only one nurse (3%) found it more difficult (score 2) than expected. Twenty-eight nurses (93%) found the redesigned fertility pen injector easy to learn and believed it

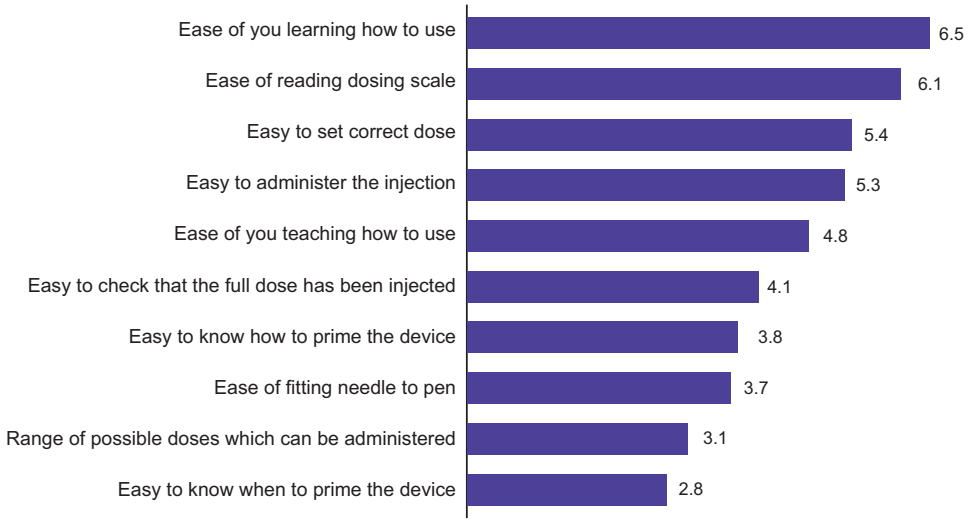

Figure 1. Top-ten attributes of pen injectors that nurses considered to be the most important; scores are mean ranking scores out of ten for each attribute.

Table 3. Features of the redesigned fertility pen injector that nurses predicted could lead to errors.

Feature leading to errors	Mentions
Dialing the dose correctly	11
Dose-feedback window too small	7
Having to split the dose	6
Not injecting full amount	4
Using a vial and syringe	3
Don't press knob far enough	2

Only features mentioned by more than one nurse are included.

Table 4. Aspects of the injection process that nurses predicted would cause the most patient anxiety.

Aspects causing anxiety	Mentions
Adjusting/setting the dose	20
Uncertainty around whether the full dose had been administered	8
Pain/bleeding/bruises after injection	4
Attaching the needle	4
Injection-site rotation	3
Scheduling of injections	2
Pen usage	2
Number of steps to follow	2
Pen storage	1
Medicine storage	1
Risk of needle-stick injuries	1

Data show the number of nurses mentioning each aspect.

would be easy to teach; one nurse (3%) thought it would be difficult to learn and to teach patients to use the redesigned infertility pen injector, and one nurse (3%) thought it would be difficult to teach patients. Almost all nurses (29/30 [97%]) would recommend the redesigned fertility pen injector to a colleague.

3.3.2. Attaching the needle (step 3)

Twenty-nine nurses (97%) found it easy to attach the needle, and 25 nurses (83%) found it easy to know whether the redesigned fertility pen injector needed to be primed (Figure 3). Twenty nurses (67%) found it easier than expected (score 4 or 5) to teach patients how to attach the needle, and 21 nurses (70%) found it easier than expected (score 4 or 5) to teach patients how to prime the redesigned fertility pen injector. One nurse (3%) found teaching patients how to attach the needle to be more difficult than expected (score 2), and two nurses (7%) found teaching patients how to prime the redesigned fertility pen injector to be more difficult (score 2) than expected.

3.3.3. Dial your dose (step 4)

All nurses found it easy (score 4 or 5) to set the dose and to teach patients how to calculate and set the dose (Figure 3). One nurse (3%) found reading the number on the dial difficult (score 2); however, this was not reflected in the nurse opinions of teaching, in which no nurses reported difficulty (score 1 or 2) when teaching patients how to read the dose-feedback window. Twenty-seven nurses (90%) found teaching patients how to calculate and set the dose easier than they expected (score 4 or 5), and 22 (73%) found teaching patients how to read the dose-feedback window easier than expected (score 4 or 5). One nurse (3%) found it more difficult (score 2) than expected to teach patients to calculate and set the dose, and one nurse (3%) found teaching patients how to read the dose-feedback window more difficult (score 2) than expected.

3.3.4. Inject your dose (step 5)

All nurses found it easy (score 4 or 5) to inject the dose and to know when the injection was complete (Figure 3). Furthermore, all nurses found it easy (score 4 or 5) to teach patients how to push the dose-setting knob. Twenty-one nurses (70%) found it easier than expected (score 4 or 5) to teach patients to push the dose-setting knob, with only two nurses (7%) finding this more difficult (score 2) than expected.

3.3.5. Remove and discard needle (step 6)

Twenty-nine (97%) nurses found removing the needle easy (score 4 or 5), with none reporting any difficulty (Figure 3). No nurses found it difficult to teach patients how to remove and discard the needle (scores 1 or 2), with 17 nurses (57%) finding this easier to teach (score 4 or 5) than expected. Three nurses (10%) found this more difficult (score 1 or 2) to teach than expected.

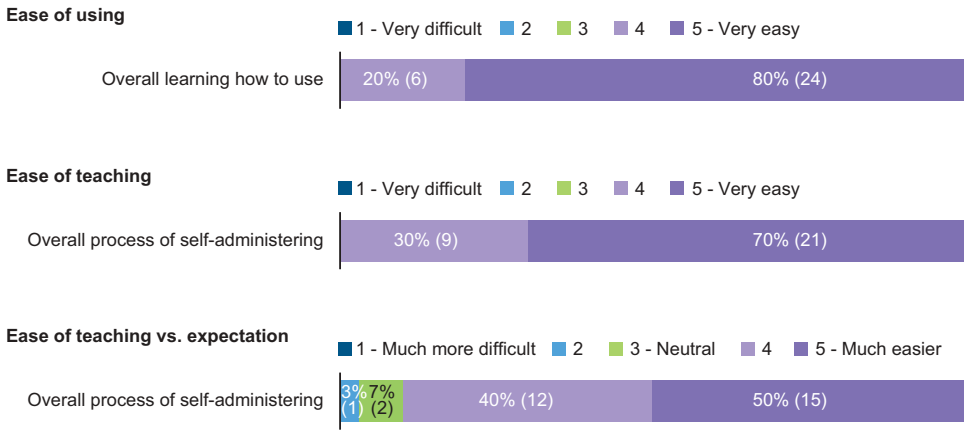

Figure 2. Overall process of self-injection. Ratings for overall ease of learning how to use, overall ease of teaching patients to self-administer, and overall ease of teaching compared with expectations ($N = 30$).

3.3.6. Complete an incomplete dose if necessary (appendix A)

Twenty-seven nurses (90%) found it easy (score 4 or 5) to know how much more dose was required to complete an incomplete injection (Figure 4) and one nurse (3%) found this task difficult (score 2). Twenty-seven nurses (90%) found it easy (score 4 or 5) to teach patients how to calculate the additional dose that was required, with the same number reporting that this was easier to teach than they anticipated (score 4 or 5); two nurses (7%) found this to be more difficult to teach than expected (score 2).

4. Discussion

The previous fertility pen injector was redesigned to improve the readability of the dose-feedback window, increase robustness and simplify handling, as part of a continuous improvement program based on user feedback [15] and human factors engineering evaluations [24,25]. The associated IFU and teaching materials were revised to improve ease of use and effectiveness, and the repertoire of drugs that can be used with the redesigned fertility pen injector now includes GONAL-f and the liquid formulation of Pergoveris.

Fertility nurse assessment of the ease to use and to teach patients to use new or modified pen injectors provides crucial input into the continual development of these devices. The study cohort comprised nurses from four European countries who taught between two and five patients in total how to use the redesigned fertility pen injector during the study. Overall, the fertility nurses considered the redesigned fertility pen injector to be both easy to use and easy to teach patients to use. Ninety percent (27 of 30) of the nurses found the overall process of teaching patients to use the redesigned fertility pen injector to be easier than anticipated. Furthermore, none of the nurses reported difficulty in teaching patients on how to calculate and set the dose, read the dose-feedback window or calculate any additional dose required following an incomplete injection. These were also the main aspects of the process that nurses found easier or much easier to teach than they anticipated. Three nurses found removing and discarding the needle more difficult than expected; however, this may be explained by the unfamiliarity of some of the nurses with the one-handed needle recapping method that was introduced in line with health authority recommendations for recapping the needle before discarding [29].

Nurses' expectations of the ease of teaching and their actual experience were least aligned for calculating an additional dose, with 90% (27 of 30) finding this easier or much easier to teach than expected (Figure 4). Any disparity between expectations and actual experience may also have arisen from preconceptions owing to previous experience when teaching patients to use other pen injectors.

Owing to the consistency of the results among the regions in the study, the findings of this study should be widely generalizable across different cultures and clinical practices. Furthermore, the results presented here were in keeping with the nurses' experiences with the previous version of the pen injector [30]. During this previous assessment, nurses found that setting and injecting the dose were uncomplicated and easy to achieve, and that the display clearly indicated whether or not a complete dose had been delivered.

These results are part of a wider study in which the ease of learning to use and subsequent ease of use of the redesigned fertility pen injector by women with recent or current infertility requiring ART or IVF were also investigated. Their overall impressions of learning to use and of using the redesigned fertility pen injector were also investigated [27]. Similar to the experience of the nurses, most of the women with infertility found all aspects of the injection process easy to learn and easy to perform. After teaching, most women felt confident they could self-administer without further teaching. Indeed, overall, nurses overestimated the level of patient anxiety for most of the tasks, and treatment-experienced patients were more anxious about the injection process than treatment-naïve patients [27].

The findings in the nurse and patient evaluation studies follow on from formative and summative usability human factors engineering evaluations of the redesigned fertility

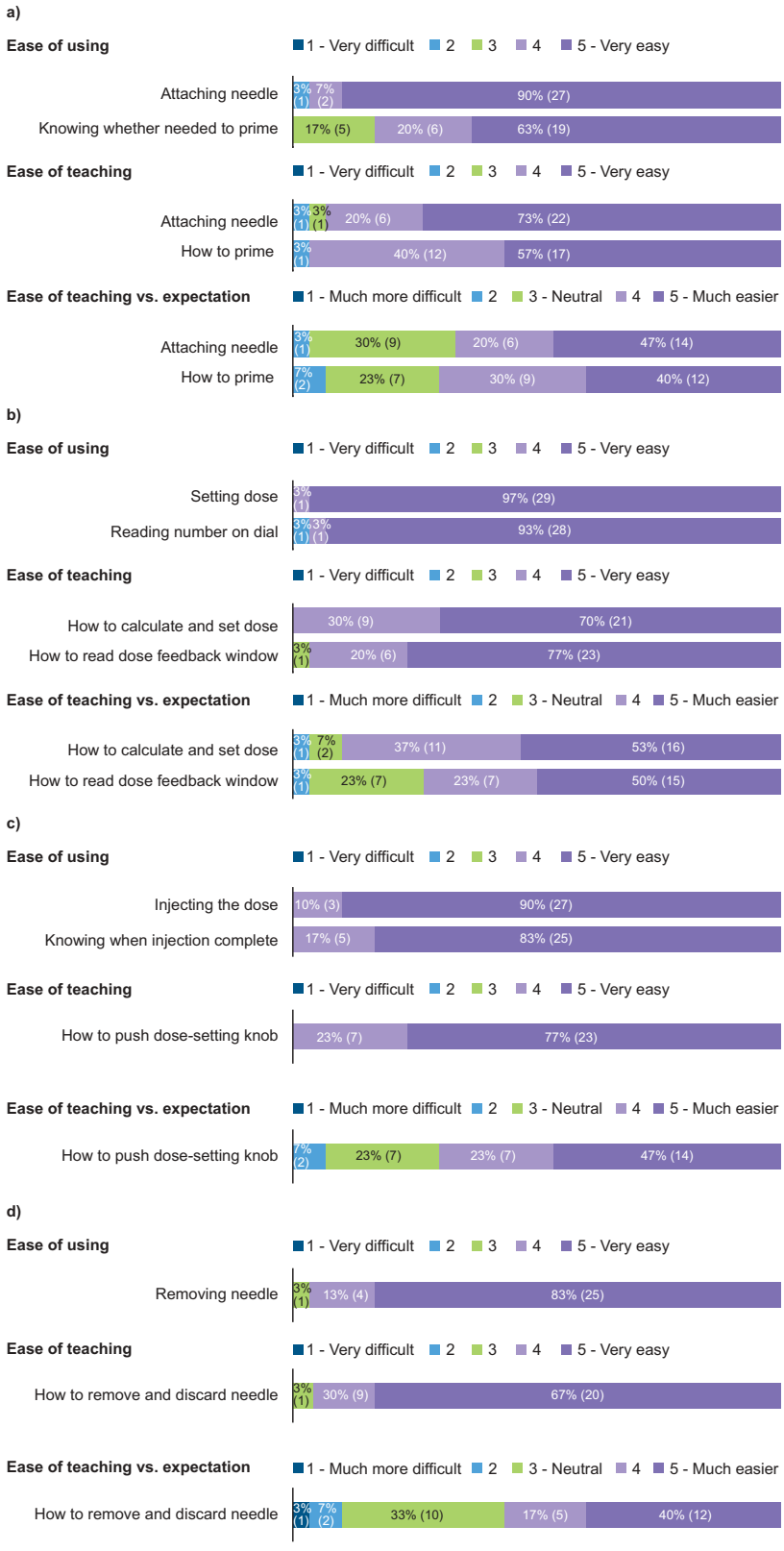

Figure 3. (a) Step 3: Attach your needle and prime the redesigned fertility pen injector. Ratings for ease of attaching the needle and knowing whether to prime, ease of teaching patients to attach the needle and how to prime, and ease of teaching compared with expectations. (b) Step 4: Dial your dose. Ratings for ease of setting the dose and reading the number on the dial, ease of teaching patients to calculate and set the dose and reading the dose in the dose-feedback window, and ease of teaching compared with expectations. (c) Step 5: Inject your dose. Ratings for ease of injecting the dose and knowing when the injection is complete, ease of teaching patients how to push the dose-setting knob, and ease of teaching compared with expectations. (d) Step 6: Remove and discard needle. Ratings for ease of removing the needle, ease of teaching patients how to remove and discard the needle, and ease of teaching compared with expectations. $N = 30$ Owing to the rounding of proportions for clarity, the responses for some categories may not add up to 100%.

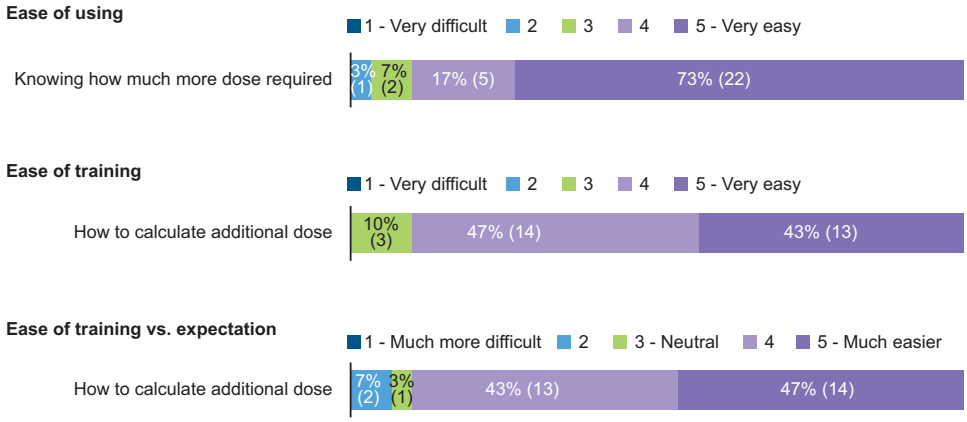

Figure 4. Appendix A: Complete an incomplete dose if necessary. Ratings for ease of knowing how much more dose is required, ease of teaching patients how to calculate an additional dose, and ease of teaching compared with expectations.

N = 30

pen injector [20]. Overall, the data presented in this manuscript, in combination with the formative and summative human factors engineering assessments, the usability assessments and the patient-experience data, represent the sum of testing that has been invested to ensure that the redesigned fertility pen injector can be used safely and effectively.

This study has a number of limitations that should be taken into consideration when interpreting the results. First, there was no delay period between teaching and use, so this simulated study does not represent the real-world situation. Furthermore, although the testing was blinded, all of the nurses had a high level of familiarity with previous versions of the pen injector, which may have facilitated the teaching and teaching procedures, and any difficulties they might have previously encountered may have led to bias. Finally, no active comparator devices were included, and any comparisons with other pen injectors may be affected by recall bias. However, any such preconceptions should have been minimized as the nurses had experience of several different devices, including the earlier versions of the pen injector, available prior to 2016.

5. Conclusions

Overall, the redesigned fertility pen injector was considered easy to use and also easy to teach patients to use. Most nurses would recommend the redesigned fertility pen injector to their colleagues and most nurses found it easier to teach patients to use the redesigned fertility pen injector than they had anticipated. The inclusion of nurses from four countries and the consistency of the results across these regions highlight the generalizability of our findings.

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Declaration of interest

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